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Title

Evaluation of coping as a mediator of the relationship between stressful life events and cancer-related distress.

Permalink

<https://escholarship.org/uc/item/0675g0jr>

Journal

Health psychology : official journal of the Division of Health Psychology, American Psychological Association, 36(12)

ISSN

0278-6133

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Publication Date

2017-12-01

DOI

10.1037/hea0000524

Peer reviewed



Published in final edited form as:

Health Psychol. 2017 December ; 36(12): 1147–1160. doi:10.1037/hea0000524.

EVALUATION OF COPING AS A MEDIATOR OF THE RELATIONSHIP BETWEEN STRESSFUL LIFE EVENTS AND CANCER-RELATED DISTRESS

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Abstract

OBJECTIVE—Lifetime stressful life events (SLEs) may predispose oncology patients to cancer-related distress (i.e., intrusive thoughts, hyperarousal, avoidance). Coping may influence cancer-related distress by mediating this relationship. This study sought to: 1) determine the prevalence and impact of lifetime SLEs among oncology outpatients receiving chemotherapy and 2) examine the relationship between SLEs and cancer-related distress and the mediating role of coping on this relationship.

METHODS—Patients (n=893), with breast, gastrointestinal, gynecologic or lung cancer, who were undergoing chemotherapy, completed the Life Stressor Checklist-Revised (LSC-R), a measure of lifetime SLEs. Cancer-related distress was assessed with the Impact of Event Scale-Revised (IES-R). Coping strategies since beginning chemotherapy were assessed with the Brief COPE; two latent variables (engagement and disengagement coping) were identified based on these scores. LSC-R scores (number of SLEs and perceived impact during the prior year) were evaluated in relation to demographic and clinical characteristics. Structural equation modeling was

used to evaluate the relationship between LSC-R and IES-R scores and the mediating role of engagement and disengagement coping on this relationship.

RESULTS—On average, patients reported 6.0 (standard deviation 4.0; range 0–23 out of 30) SLEs. Patients who were not married/partnered, lived alone, had incomes <\$30,000/year, or who had lower functional status or greater comorbidity had higher LSC-R scores. The relationship between more SLEs and more severe cancer-related distress was completely mediated by disengagement coping. Engagement coping did not mediate this relationship.

CONCLUSIONS—Disengagement coping, including behavioral disengagement, avoidance, and denial, should be targeted to mitigate cancer-related distress.

Keywords

oncology; cancer; chemotherapy; distress; life stressors; coping

INTRODUCTION

Cancer-related distress, namely, the experience of cancer-specific, post-traumatic stress symptoms (i.e., intrusive thoughts, autonomic hyperarousal, avoidance), is common in oncology patients and cancer survivors (Cordova et al., 1995; Gold et al., 2012; Mehnert & Koch, 2007; Thekdi et al., 2015; Waldrop, O'Connor, & Trabold, 2011) and has numerous deleterious effects on symptom burden, functional status, and quality of life (QOL) (Cordova, et al., 1995; Gold, et al., 2012; Thekdi, et al., 2015; Yanez, Garcia, Victorson, & Salsman, 2013). In a minority of patients, cancer-related distress reaches the threshold for a diagnosis of post-traumatic stress disorder (PTSD), and another subgroup appears to suffer sub-threshold or subclinical post-traumatic stress symptoms (PTSS) (Shand, Cowlshaw, Brooker, Burney, & Ricciardelli, 2015). However, the majority of patients do not experience PTSS or PTSD, highlighting the heterogeneity of cancer-related distress (Cordova & Andrykowski, 2003).

Efforts to predict who is at increased risk for higher levels of cancer-related distress have focused on disease, treatment, sociodemographic, and psychological variables as predictors. Factors associated with higher levels of cancer-related distress included younger age (Cordova, et al., 1995), diagnostic delay (Miles et al., 2016), higher levels of preoperative anxiety and acute postoperative pain (Jeantieu et al., 2014), lower self-efficacy (Kohno et al., 2010), difficulty tolerating uncertainty (Eisenberg et al., 2015), lower social support (Carpenter, Fowler, Maxwell, & Andersen, 2010), and higher trait anxiety (Ristvedt & Trinkaus, 2009).

Only a few studies have examined the relationship between pre-cancer stressful life events (SLEs) and cancer-related distress. For instance, Mehnert and colleagues found that a prior history of PTSD conferred a significantly higher likelihood of developing an acute stress disorder or PTSD after a breast cancer diagnosis (Mehnert & Koch, 2007). Similarly, among women newly diagnosed with breast cancer, a history of childhood emotional abuse was independently associated with cancer-related intrusive symptoms (Goldsmith et al., 2010). In addition, among women with metastatic breast cancer, a higher number of SLEs was

associated with higher levels of cancer-related intrusive thoughts and avoidance (Butler, Koopman, Classen, & Spiegel, 1999).

Building on the foundation of Andersen's biobehavioral model of cancer stress and disease course (Andersen, 1993; Andersen, Kiecolt-Glaser, & Glaser, 1994) in which disease, treatment, demographic, social, and psychological variables affect risk for psychological symptom morbidity, Andrykowski and colleagues evaluated predictors of PTSD symptoms among breast cancer survivors (n=82). These authors reported that the addition of premorbid traumatic stressors to the variables suggested by Andersen's model helped explain a greater amount of the variance in PTSD symptoms (Andrykowski & Cordova, 1998). Cordova and Andrykowski later proposed a distinct model conceptualizing cancer as a "psychosocial transition." Their model challenged the assumption that cancer is a traumatic stressor for all patients, based on empiric literature on both post-traumatic symptoms as well as post-traumatic growth among cancer patients. While Andersen's biobehavioral model and Cordova and Andrykowski's "psychosocial transition" model provide useful conceptual starting points, neither theorizes regarding potential mechanisms linking SLEs and cancer-related distress.

In contrast, the broadly-based, empirically well-validated model of "coping as a process" (Lazarus & Folkman, 1984) helps us conceptualize how SLEs may relate to cancer-related distress. Specifically, they define coping as "constantly changing cognitive and behavioral efforts to manage specific external and/or internal demands that are appraised as taxing or exceeding the resources of the person" (Lazarus & Folkman, 1984). Coping is explicitly distinguished as a process, not an outcome, in this model. Furthermore, coping as a process provides a theoretical link between efforts to manage longer-term stressors (e.g., cumulative SLEs) with more immediate efforts to manage near-term stressors (e.g., cancer treatment).

Across studies that examined coping in relation to psychological outcomes in cancer patients, engagement (also called adaptive or problem-focused) forms of coping (e.g., positive reframing, seeking support) were associated with lower levels of psychological distress and better QOL. In contrast, disengagement (also called maladaptive or emotion-focused) forms of coping (e.g., avoidance, denial) were associated with higher levels of psychological symptoms (e.g., anxiety, depression, post-traumatic stress) and worse QOL (Carver et al., 1993; Heim, Valach, & Schaffner, 1997; Lutgendorf et al., 2000; McCaul et al., 1999; Roesch et al., 2005; Shapiro, McCue, Heyman, Dey, & Haller, 2010).

Given the prior work that demonstrates a relationship between SLEs and cancer-related distress, and the theoretical mediating role of coping in this relationship, we sought to better characterize and understand SLEs and their impact among a sample of patients undergoing chemotherapy (CTX; n=893). Because prior studies that examined SLEs in relation to cancer-related distress have not characterized the prevalence and impact of lifetime SLEs on patients' current lives or examined differences in SLEs with respect to demographic and clinical characteristics, we first sought to characterize the prevalence, types, and impact of SLEs using a valid and reliable self-report inventory of lifetime stressful events, the Life Stressor Checklist-Revised (LSC-R) (McHugo et al., 2005; Wolfe & Kimmerling, 1997). Next, we evaluated for differences in the number and impact of SLEs with respect to

demographic and clinical characteristics. Finally, we examined the relationship between SLEs and cancer-related distress and evaluated the potential mediating roles of engagement and disengagement forms of coping used since beginning CTX treatment on this relationship. Based on the process model of coping, as well as on existing literature on the mediating effects of coping (Carver, et al., 1993; Roesch, et al., 2005; Shapiro, et al., 2010), we hypothesized that both engagement and disengagement coping strategies would mediate the relationship between SLEs and cancer-related distress.

METHODS

Patients and settings

This study included patients who were part of a larger, longitudinal study that evaluated the symptom experience of oncology outpatients receiving CTX (Kober, Cooper, et al., 2016; Kober, Dunn, et al., 2016; Langford et al., 2016; Wright et al., 2015). Eligible patients were 18 years of age; had a diagnosis of breast, gastrointestinal, gynecological, or lung cancer; had received CTX within the preceding four weeks; were scheduled to receive at least two additional cycles of CTX; were able to read, write, and understand English; and gave written informed consent. Patients were recruited from two Comprehensive Cancer Centers, one Veteran's Affairs hospital, and four community-based oncology programs. A total of 1486 patients were approached and 893 consented to participate (60.1% response rate). The major reason for refusal was being overwhelmed with their cancer treatment.

Instruments—A demographic questionnaire obtained information on age, gender, ethnicity, marital status, living arrangements, education, employment status, and income.

The Karnofsky Performance Status (KPS) scale is widely used to evaluate functional status in patients with cancer and has well established validity and reliability (Karnofsky, Abelmann, Craver, & Burchenal, 1948). Patients rated their functional status using the KPS scale that ranged from 30 (I feel severely disabled and need to be hospitalized) to 100 (I feel normal; I have no complaints or symptoms) (Karnofsky, 1977; Karnofsky, et al., 1948).

The LSC-R is a 30-item inventory of lifetime exposure to stressful events, including potentially traumatic events (e.g., being mugged, the death of a loved one, a sexual assault) (Schumacher et al.; Wolfe & Kimmerling, 1997). The total LSC-R score was obtained by adding up the number of events endorsed (possible range 0–30, with 30 indicating that the individual experienced all events). If the patient endorsed an event, the patient was asked to indicate how much that stressor affected his/her life in the past year, from 1 (“not at all”) to 5 (“extremely”). These responses were averaged to yield a mean “Affected” score. The LSC-R has demonstrated good to moderate test–retest reliability and good criterion-related validity with diverse populations (Humphreys, Cooper, & Miaskowski, 2010; Kimerling et al., 1999; Lawson, Back, Hartwell, Moran-Santa Maria, & Brady, 2013; Mahoney et al., 2015).

The Brief COPE is a 28-item instrument that was designed to assess a broad range of coping responses among adults (Carver, 1997; Carver, Scheier, & Weintraub, 1989). For this study, patients were asked to rate to what extent they were utilizing each coping strategy since

beginning CTX. Each item is rated on a four-point Likert scale that ranged from 1 (“I haven’t been doing this at all”) to 4 (“I have been doing this a lot”). Higher scores indicate greater use of the various coping strategies. In total, 14 dimensions, each assessed using two items, were evaluated using this instrument (with their respective Cronbach’s alphas from the present study), namely: self-distraction (0.46), active coping (0.75), denial (0.72), substance use (0.87), use of emotional support (0.77), use of instrumental support (0.77), behavioral disengagement (0.57), venting (0.65), positive reframing (0.79), planning (0.74), humor (0.83), acceptance (0.68), religion (0.92), and self-blame (0.73). The Brief COPE has well-established validity and reliability in oncology patients (Scrignaro, Barni, & Magrin, 2011; Yusoff, Low, & Yip, 2010).

The Impact of Event Scale-Revised (IES-R) is a 22-item instrument that was used to measure cancer-related distress (Horowitz, Wilner, & Alvarez, 1979; Weiss & Marmar, 1997). Developed to assess an individual’s thoughts, feelings, and behaviors in response to specific, potentially traumatic events (e.g., assault, serious illness), the IES-R was used in a number of studies to evaluate cancer-related distress (Chambers, Zajdlewicz, Youlden, Holland, & Dunn, 2014; Eisenberg, et al., 2015; Kohno, et al., 2010; Mehnert & Koch, 2007). Patients rated each item based on how distressing each potential difficulty was for them during the past week with respect to their cancer and its treatment. Each item was rated on a scale from 0 (‘not at all’) to 4 (‘extremely’). Three subscales (intrusion [e.g., “Any reminder of it brought back feelings about it”]; avoidance [e.g., “I tried not to think about it”]; hyperarousal [e.g., “I felt watchful and on-guard”]) and a total score are created by summing their respective items. The total score can range from 0 to 88. Scores above 24 suggest at least “partial” (or subthreshold) PTSD, while a cut-off of 33 or greater represents probable PTSD, and scores of 37 or greater suggest high levels of post-traumatic symptoms (Weiss & Marmar, 1997). The IES-R has well-established validity and reliability (Civilotti et al., 2015; Creamer, Bell, & Failla, 2003; Sundin & Horowitz, 2002). In this study, the Cronbach’s alpha for the IES-R total score was 0.92.

Study procedures

The study was approved by the Committee on Human Research at the University of California, San Francisco and by the Institutional Review Board at each of the study sites. Eligible patients were approached by a research staff member in the infusion unit to discuss participation in the study. Written informed consent was obtained from all patients. Medical records were reviewed for disease and treatment information.

Due to the potentially sensitive nature of LSC-R items, patients were given three options for its completion: in person with a research staff member, over the telephone, or on their own. Two patients chose to complete the LSC-R in person. The remainder completed it on their own. Patients were reminded that they could refuse to answer questions that caused discomfort. A list of relevant psychosocial resources was available for patients if any distress was expressed. None of the patients related any concerns or adverse events regarding the LSC-R to the research team. Patients completed all other self-report instruments without assistance.

Data analysis

LSC-R descriptive statistics—Descriptive statistics and frequency distributions were calculated for demographic and clinical characteristics. Frequency distributions were generated for each LSC-R item. Descriptive statistics were generated for the total number of life stressors endorsed, as well as the mean impact of each item on the patient's life in the past year.

Bivariate correlations, independent samples t-tests, and one-way analyses of variance with Bonferroni adjusted post-hoc contrasts were used to determine differences in LSC-R scores (i.e., Total and Affected scores) by demographic and clinical characteristics. Data were analyzed using Stata/SE Version 14 (StataCorp., 2015). Significance tests were evaluated with a two-sided alpha of .05.

Structural equation modeling—The association between cancer-related distress (as measured by IES-R total score) and SLEs (measured by LSC-R total score) was examined in a series of structural equation models (SEM) that estimated the direct and indirect (mediating) effects of SLEs on cancer-related distress via both engagement and disengagement coping (as measured by specified subscales of the Brief COPE, as described below). Specifically, four SEMs were estimated to evaluate: the direct effect of life stress and coping on cancer-related distress (Model 1); the mediating effect of engagement coping on the relationship between life stress and cancer-related distress (Model 2); the mediating effect of disengagement coping on the relationship between life stress and cancer-related distress (Model 3); and the mediating effect of both engagement and disengagement coping on the relationship between life stress and cancer-related distress (Model 4). Certainly, a myriad of factors may influence patients' cancer-related distress; however, an evaluation of all potential covariates was outside the scope of the current study. In an effort to address specifically and parsimoniously the research question of whether the relationship between cumulative life stress (predictor) and cancer-related distress (outcome) is mediated by engagement and/or disengagement coping (mediators), we elected to include only these variables in the model.

Cancer-related distress was estimated as a latent variable derived from the observed IES-R total score, taking measurement error into account (Jøreskog & Sörbom, 1993). Exploratory factor analysis (EFA) on the 14 subscales of the Brief COPE was used to better characterize coping strategies. After removal of poorly-loading and cross-loading factors, EFA identified two distinct coping categories, each comprised of three subscale scores from the Brief COPE. These factors were used to estimate coping strategies in the structural models. "Engagement coping" was estimated as a latent variable from three observed subscales: active coping, positive reframing, and utilization of emotional support. "Disengagement coping" was estimated as a latent variable from three observed subscales of the Brief COPE: self-blame, denial, and behavioral disengagement. Although the simple associations of LSC-R total score, engagement coping, and disengagement coping with distress were expected to be significant, we were particularly interested in determining whether the associations between the LSC-R total score and distress would be reduced partially or completely when

the indirect (mediating) effects of engagement coping and disengagement coping were included in the SEM.

Estimation for the structural models was carried out using Mplus Version 7.4 (L. K. Muthen & Muthen, 1998–2015) with robust maximum likelihood. Robust full information maximum likelihood (robust FIML) reduces or eliminates bias in estimates that may be due to non-normal distributions of observed variables (L. K. Muthen & Muthen, 1998–2015).

Missing data for distress, life stress, and the Brief COPE measures were accommodated by FIML and the Expectation Maximization (EM) algorithm. An advantage of estimation using FIML and the EM algorithm is that effects can be estimated with all cases even if measures are missing for some cases (Enders, 2010; B. Muthen & Shedden, 1999; J. L. Schafer & Graham, 2002). This method provides unbiased parameter estimates provided that the missingness is “ignorable” (Enders, 2010; McKnight, McKnight, Sidani, & Figueredo, 2007; J.L. Schafer, 1997; J. L. Schafer & Graham, 2002). This assumption is reasonable for the current study, because missingness should be associated with other measures of the outcome or covariates. Some missingness might be “missing completely at random” for reasons that have nothing to do with the study or the predictor or outcome variables.

It is known that indirect (mediating) effects are typically not normally distributed. Therefore, estimation of the indirect effects was carried out using a nonparametric bootstrap with 5,000 draws. These results are reported with bias-corrected confidence intervals following the recommendations of Shrout & Bolger (Shrout & Bolger, 2002).

Four types of fit indices were used to evaluate competing models: absolute fit, fit adjusting for model parsimony, comparative fit, and the Bayesian Information Criterion (BIC) (Brown, 2015; Kline, 2015; L. K. Muthen & Muthen, 1998–2015; Raykov & Marcoulides, 2006). Absolute fit was estimated with the standardized root mean square residual (SRMR: average discrepancy between the observed and predicted correlation matrix; should be $<.08$) (Hu & Bentler, 1998, 1999). Model parsimony was estimated with the root mean square error of approximation (RMSEA; while the preference is that the RMSEA $<.06$; close fit is $<.05$; adequate fit is $<.08$ (Browne & Cudeck, 1993); mediocre fit is between $.08$ and $.10$ (MacCallum, Browne, & Sugawara, 1996)). Comparative fit was estimated with the comparative fit index (CFI; while a CFI $>.95$ is preferred, $>.90$ is acceptable (Bentler, 1990; Hu & Bentler, 1998, 1999; Kline, 2015)). Finally, the Chi-square test for goodness of fit was estimated. However, this index for absolute fit is not useful based on the significance test, because it will almost always be significant when the sample size is large enough to estimate a complex model (more than two hundred observations), even for a well-fitting model. Therefore, the BIC was employed to compare competing models (Acock, 2013; Kline, 2015; L. K. Muthen & Muthen, 1998–2015; Raykov & Marcoulides, 2006). The BIC provides an adjustment to the -2Log Likelihood (on which the Chi-squared test of model fit is based) that corrects for the number of patients and the number of parameters in the model.

Descriptive and preliminary analyses were carried out with Stata/SE Version 14 (StataCorp., 2015). Significance tests were evaluated with a two-sided alpha of $.05$.

RESULTS

Patient characteristics

Table 1 summarizes the demographic, clinical, and psychological characteristics of the 893 patients. On average, patients were 57 years old, college-educated, and had a mean KPS score of 80.5. The majority of patients were female, white, married/partnered, not currently working, and had metastasis to another site (i.e., including lymph nodes).

Frequency and impact of stressful life events (SLEs)

Patients reported a mean of 6.0 SLEs (± 4.0 ; range 0–23 out of 30) and a total mean impact of 1.8 (± 0.9 ; range 1–5). Table 2 displays the SLEs in order of descending frequency (i.e., % of patients who endorsed each item). The five most frequently reported stressors were the death of someone close (not sudden: 78.2%; sudden: 50.0%), having an abortion or miscarriage (44.5%), being in a serious disaster (41.0%), and being separated or divorced (35.4%). In addition, Table 2 displays the mean perceived effect of the event on one's life during the past year from 1 ("not at all") to 5 ("extremely") and the ranking of stressors by impact (i.e., Affected Ranking). The stressor with the most significant recent impact was having a child with a physical or mental handicap (mean = 3.16 ± 1.4), followed by a patient-specified stressor not addressed by the inventory (mean = 3.15 ± 1.5), and physical neglect (mean = 2.76 ± 1.3). Note that a score of 3 corresponds to "some" effect on one's life in the past year.

Demographic and clinical characteristics by LSC-R scores

Table 3 describes differences in LSC-R scores associated with a number of demographic and clinical characteristics. LSC-R total scores did not differ significantly by gender. Although age was not associated with the total number of stressful life events, younger age was associated with a higher mean effect of SLEs during the past year ($p=0.02$). LSC-R total scores ($p<0.001$), but not affected scores ($p=0.05$), differed significantly with respect to self-reported race/ethnicity. Asian patients reported significantly fewer life stressors than other racial groups ($p<0.001$). In addition, patients of "Other" ethnicities (i.e., a variable that combined participants who self-reported as American Indian/Alaskan native, mixed ethnic background, native Hawaiian/other Pacific Islander, or other) reported a significantly higher number of SLEs than did White patients ($p = 0.004$).

Both LSC-R total and affected scores differed with respect to income ($p<0.001$). Patients with a gross annual household income of $< \$30,000$ reported significantly more SLEs than patients with an annual income of $> \$30,000$ (all $p<0.05$). Patients with an annual income of $< \$30,000$ reported a greater impact of SLEs on recent life than patients with an annual income of $> \$70,000$; and those with an annual income $< \$70,000$ reported a greater impact than those with an annual income $> \$100,000$ (both $p<0.05$). Patients who were not married or partnered reported significantly more SLEs and a greater impact on recent life than those who were married/partnered (both $p<0.001$).

In terms of clinical characteristics, the presence of metastatic disease was not significantly associated with the number ($p=0.32$) or impact ($p=0.32$) of SLEs. A lower functional status

was associated with a higher number and a greater impact of SLEs (both $p < 0.001$). Higher comorbidity scores were associated with a higher number and greater impact of SLEs (both $p < 0.001$).

Results of structural equation modeling

Table 4 provides descriptive statistics for the variables in the joint mediation model and for the correlations among the variables in the model. The cancer-related distress (IES-R total) and life stress (LSC-R total) scores were rescaled by dividing by 10, in order to reduce the size of the variances and covariances and improve model fit (L. K. Muthen & Muthen, 1998–2015). Missing data for the outcome and the Brief COPE scales used to define the engagement and disengagement coping latent variables were accommodated by FIML and the EM algorithm. However, 53 cases that were missing the primary predictor (LSC-R score) were excluded from the analysis. Model fit, evaluated using the BIC, was better (more than 200 points lower) for the model that did not include cases with missing data for the primary predictor. Therefore, the structural model was estimated with 893 cases with nonmissing data on their LSC-R score and who provided responses to at least one of the dependent variables in the model (i.e., the coping variables and the IES-R score).

Measurement model—The measurement models for engagement coping and disengagement coping demonstrated that the three subscale scores for each type of coping provided significant contributions to the latent variables (see Table 5). As can be seen from the standardized coefficients, while active coping and positive reframing contributed most strongly to engagement coping, emotional support provided a significant contribution. While self-blame provided the strongest contribution to disengagement coping, both denial and behavioral disengagement made significant contributions. To improve model fit, correlated residuals were allowed between denial and behavioral disengagement. (The item contents for the two subscales are very similar, so some of the subscale variance is likely to be shared beyond the portion that defines the disengagement coping latent variable.) As described previously, cancer-related distress was estimated as a latent variable following the procedure recommended by Jøreskog and Sörbom (1993), which specified the measurement error for the observed IES-R total score computed from $1 - \text{the alpha reliability for the scale } (.91)$.

SEM—Model 1 (Figure 1A), which evaluated the direct effect of life stress, engagement coping, and disengagement coping jointly (but with no paths for mediation) on cancer-related distress, revealed significant paths for life stress and disengagement coping to cancer-related distress, but not for engagement coping.

For Model 2 (Figure 1B), which evaluated the mediating effect of engagement coping on the relationship between life stress and cancer-related distress, the direct effect of life stress on cancer-related distress was significant. Engagement coping was not a significant predictor of cancer-related distress in this simple model, nor was there a significant indirect effect of life stress on cancer-related distress via engagement coping.

For Model 3 (Figure 1C), which evaluated the mediating effect of disengagement coping on the relationship between life stress and cancer-related distress, life stress was associated with disengagement coping, and disengagement coping was associated with cancer-related

distress. However, the direct effect (path) from life stress to cancer-related distress was not significant. In the simple mediation model employing disengagement coping, the indirect effect of life stress on cancer-related distress via disengagement coping was significant (coefficient .717, bootstrapped confidence interval [CI] .238 to 2.231).

Finally, the structural model that evaluated the joint mediating effects of engagement and disengagement coping (Model 4, Figure 1D) depicts the hypothesis that cancer-related distress would be associated with life stress, engagement coping, and disengagement coping. As depicted in the mediation model (Model 4, Figure 1D) and described in Table 6, life stress did not have a significant direct relationship with cancer-related distress (path coefficient $-.036$, $p=.875$). The direct effects of life stress on each of the mediators were both significant (engagement coping $.302$, $p=0.01$, and disengagement coping $.346$, $p=0.007$). While engagement coping did not predict cancer-related distress ($-.032$, $p=.561$), disengagement coping did predict cancer-related distress (2.068 , $p=0.004$). As shown in Table 6, life stress *did* have a significant indirect (mediating) effect on cancer-related distress via disengagement coping (coefficient= 0.716 , bootstrapped CI $.238$ to 2.244), even though its direct effect was weak and non-significant. That the direct effect of life stress was significant in a model with no mediating effects, but not significant in the model with joint mediating effects, indicates complete mediation. That is, the effect of life stress on cancer-related distress can be explained almost completely by patients' levels of disengagement coping.

In addition, the fit indices for the joint mediation model that included the nonsignificant mediating effect of engagement coping were slightly better than for a model that included a mediating effect only for disengagement coping. Although both the CFI and SRMR showed good fit for both models, the more important RMSEA was within the desired range (<0.06) only for the full model and greater than the maximum acceptable value for the reduced model (i.e., 0.095 which is > 0.08). As such, the joint mediation model was more informative, despite the nonsignificant mediating effect of engagement coping.

DISCUSSION

This study provides a detailed description, using the LSC-R, of lifetime SLEs experienced by oncology patients, as well as the perceived impact of lifetime SLEs on patients' recent lives. This study is the first to utilize the LSC-R to characterize oncology patients' histories of SLEs. Patients reported an average of 6 SLEs over the course of their lifetime. However, on average, these stressors had a fairly mild impact on recent life (approximately 2 out of 5). Interestingly, a total LSC-R cut-off score of 6 was found to be a reliable predictor of trauma-related symptoms (Ungerer, Deter, Fikentscher, & Konzag, 2010). Thus, the present findings suggest that a substantial proportion of cancer patients are at risk for trauma-related symptoms associated with past SLEs.

The demographic characteristics associated with higher LSC-R scores were similar for both LSC-R total scores and LSC-R Affected scores. Patients who were not married or partnered or who lived alone reported significantly more stressful life events. This finding is consistent with a study of Turkish oncology outpatients (Tas et al., 2012), in which married patients

reported significantly fewer stressful events in the prior year than did their non-married counterparts. This finding may be due to the fact that “being separated or divorced” is an SLE surveyed by the LSC-R. Alternatively, this finding may be associated with an underlying predisposition to experience more life stressors and/or a lower likelihood of developing and maintaining close relationships (Birditt, Antonucci, & Tighe, 2012). In contrast, social support from a partner or others may provide a buffer against exposure to or the negative effects of stressful events (Butler, et al., 1999; Carpenter, et al., 2010; Heaney & Israel, 2008; Kornblith et al., 2001; Maly, Umezawa, Leake, & Silliman, 2005). Interestingly, findings regarding the impact of social support on coping strategies in cancer patients and survivors suggest that lower social support is associated with maladaptive coping (Zucca, Boyes, Lecathelinais, & Girgis, 2010), while greater social support may enhance coping strategies (Shapiro, et al., 2010; Zhou et al., 2010).

Consistent with findings that lower income is associated with greater physical and psychosocial stressors (Evans & English, 2002; Tas, et al., 2012), patients with annual incomes of <\$30,000 reported significantly more SLEs. Alternatively, it is possible that the impact of cumulative life stress may restrict job opportunities and impede career development. Finally, “serious money problems” is an item on the LSC-R. Therefore, patients with lower incomes would be more likely to endorse this stressor.

In the current sample, Asian patients reported significantly fewer stressful life events than other ethnic groups. This finding corroborates research that used the LSC-R to evaluate for life stressors among geographically disparate groups of women (Humphreys, J; unpublished data). This finding may be due to cultural or environmental differences that influence exposure to, disclosure of, and/or self-appraisal of such stressors. The finding that patients of “Other” ethnicities reported significantly more stressful life events than White patients should be interpreted with caution because of the small percentage (<10%) of patients in this heterogeneous group.

Two clinical variables were associated with life stress in our sample. A lower functional status and a higher level of comorbidity were associated with a greater number and impact of SLEs. This finding may reflect a predisposition to life stress among patients with poorer functional status who are coping with a number of medical comorbidities. Alternatively, stressors may take a physical toll, directly or through other mediating variables, which impedes functional status and facilitates the development of comorbid conditions. The latter hypothesis has gained considerable support from research linking, for example, early life exposure to stressful events and immune dysregulation (Fagundes, Glaser, & Kiecolt-Glaser, 2013). In any case, these patients constitute a high risk group who may be particularly vulnerable to the impact of SLEs.

An examination of the final SEM reveals some important findings. First, the use of disengagement forms of coping with cancer treatment was robustly associated with cancer-related distress. Although initial analyses found that life stress was positively associated with cancer-related distress, mediation analyses revealed that this relationship was completely mediated by disengagement coping. Moreover, while life stress was associated with

engagement coping, this potential mediator was not significantly associated with cancer-related distress.

It is interesting that life stress is associated with *both* engagement (i.e., active coping, positive reframing, emotional support) and disengagement (i.e., behavioral disengagement, denial, self-blame) coping. While SLEs can negatively impact coping (Leitenberg, Gibson, & Novy, 2004; Mc Elroy & Hevey, 2014; Nurius, Green, Logan-Greene, & Borja, 2015), a growing body of research suggests that exposure to SLEs may positively impact coping. For example, individuals have identified positive changes that have occurred as a result of a stressful or traumatic event, often referred to as “post-traumatic growth” or “benefit finding” (Barskova & Oesterreich, 2009; Cordova & Andrykowski, 2003; Danhauer et al., 2013; Helgeson, Reynolds, & Tomich, 2006; Morris & Shakespeare-Finch, 2011; Shand, et al., 2015; Tomich & Helgeson, 2004). Future research is warranted on the characteristics (including personality traits) of cancer patients who are at higher risk for the development of disengagement coping (or, conversely, less likely to use engagement coping) following exposure to SLEs (Tedeschi & Calhoun, 1996).

Given evidence in the literature that engagement coping strategies, such as “focusing on the positive,” “seeking out or using social support,” and “active problem solving” are associated with lower levels of emotional distress in oncology patients (Dunkel-Schetter, Feinstein, Taylor, & Falke, 1992; Roesch, et al., 2005), it is surprising that we did not find a negative association between engagement coping and cancer-related distress in the current sample (i.e., greater engagement coping associated with less distress). One possibility for this finding is that our latent variable for engagement coping (which combined the three Brief COPE subscales of active coping, positive reframing, and utilization of emotional support) did not access certain specific coping strategies that might be protective.

For example, several studies in cancer patients demonstrated that both acceptance and humor, measured using the Brief COPE, were associated with lower levels of distress and better adjustment to breast cancer (Carver, et al., 1993; Shapiro, et al., 2010). Moreover, because patients were reflecting on their coping strategies since beginning CTX, the specific timing of the assessment of the variables of interest (i.e., coping and distress during active treatment) may have influenced the present findings. One study of over 500 women found that emotional approach coping was only associated with better adjustment in the year following breast cancer treatment completion in women with low levels of life stress (Low, Stanton, Thompson, Kwan, & Ganz, 2006). Therefore, engagement coping may only be adaptive for a subset of patients or only after treatment is completed.

As expected, exposure to a greater number of SLEs was associated with increased cancer-related distress. However, this relationship was completely mediated by disengagement coping behaviors. At least one study, conducted in women two years after diagnosis of early stage breast cancer (n=170), found no relationship between prior life stressors and levels of cancer-related distress (measured using the original IES). However, the potential mediating role of coping was not evaluated (Bleiker, Pouwer, van der Ploeg, Leer, & Ader, 2000). Another study of women with metastatic cancer (n=125) found that women with higher

levels of past SLEs were more prone to clinically significant intrusion and avoidance symptoms related to their cancer (Butler, et al., 1999).

Moreover, disengagement coping was uniquely associated with cancer-related distress. While the association between disengagement coping and cancer-related distress was reported previously (Roesch, et al., 2005), disengagement coping as a mediator between SLEs and cancer-related distress is a novel finding. This result adds to a growing literature documenting the mediating effects of disengagement coping on the relationship between numerous types of stressors and an array of psychological outcomes (e.g., depression, anxiety, positive affect, health behaviors, physical health) (Carver & Connor-Smith, 2010; Littleton, Horsley, John, & Nelson, 2007).

Given its mediating role, disengagement coping may be an important target for interventions to alleviate cancer-related distress, particularly among patients with a history of life stress. In particular, denial, self-blame, and behavioral disengagement should be addressed. Numerous interventions that include disengagement coping as a target have been developed for both cancer and non-cancer populations (Steinhardt & Dolbier, 2008). For example, in a recent study of a group intervention designed to enhance “cognitive emotion regulation” among breast cancer patients, improvements were demonstrated in both adaptive and maladaptive coping (Hamama-Raz et al., 2016). Furthermore, specific psychotherapy approaches often utilized with cancer patients (e.g., cognitive-behavioral therapy, cognitive-behavioral stress management) attempt to target disengagement coping (e.g., through the use of behavioral activation; identifying and challenging cognitive distortions; and addressing damaging, negative core beliefs about oneself and the world). Further work in cancer patients should evaluate the mechanisms that underlie the effects of these therapeutic approaches on specific coping strategies, as well as on psychological outcomes.

Limitations of the study should be acknowledged. Because the LSC-R is retrospective, it is possible that patients’ cancer or symptom experiences influenced memory of past events. In addition, causal inferences about the various relationships identified in this study cannot be made due to the cross-sectional nature of the study. As is the case with most studies, the sample was comprised of patients willing to participate and to complete the LSC-R. The sample was largely well-educated and had, on average, a fairly high annual household income, although many were not working for pay. Therefore, it is unclear how representative this sample is of cancer patients overall. Because many patients face financial stressors during cancer treatment, the effects of socioeconomic status should be examined in future research on coping and cancer-related distress during treatment. Moreover, a substantial proportion of patients (40%) refused to participate in this study, typically due to feeling overwhelmed with their current life circumstances (i.e., cancer treatment). As such, the findings reported herein may underestimate cancer-related distress in particular and may not be an accurate reflection of the spectrum of coping skills. In addition, the instrument used to evaluate cancer-related distress consists of three subscales, each evaluating a dimension of post-traumatic stress (i.e., avoidance, hyperarousal, intrusive thoughts). For the purposes of the current paper, we elected to evaluate the total score for the instrument. Thus, the relationships among the variables evaluated may not reflect the specific components of cancer-related distress. It should be noted that factor analysis revealed two non-overlapping,

strongly loading factors that comprised six of a possible 14 subscales of the Brief COPE. It is possible that other coping strategies (e.g., venting, planning, acceptance) may play a role (Shapiro, et al., 2010). Finally, while we limited the scope of the SEM to a parsimonious evaluation of life stress, coping, and cancer-related distress, there are likely other measured or “unmodeled” factors at play.

Despite these limitations, the present findings, based on a large, heterogeneous sample of oncology outpatients undergoing CTX, illustrate the importance of not only identifying risk factors for cancer-related distress, but also examining potential mediators of the relationships among these risk factors and cancer-related distress. Moreover, the present findings suggest that the relationship between past SLEs and cancer-related distress is not straightforward, but rather is influenced by intervening variables that may be modifiable. In particular, patients whose coping strategies include behavioral disengagement, avoidance, and denial appear to be at particular risk for cancer-related distress during treatment. Whether cancer patients’ use of specific coping strategies, in turn, reflects other underlying predispositions (e.g., personality traits) warrants examination, given the non-overlapping, interactive relationships between personality traits and coping (Carver & Connor-Smith, 2010). Finally, the potential mediating roles of coping and personality on other important physical and psychological outcomes in cancer patients warrant investigation.

Acknowledgments

Funded by a grant from the National Cancer Institute (NCI CA134900).

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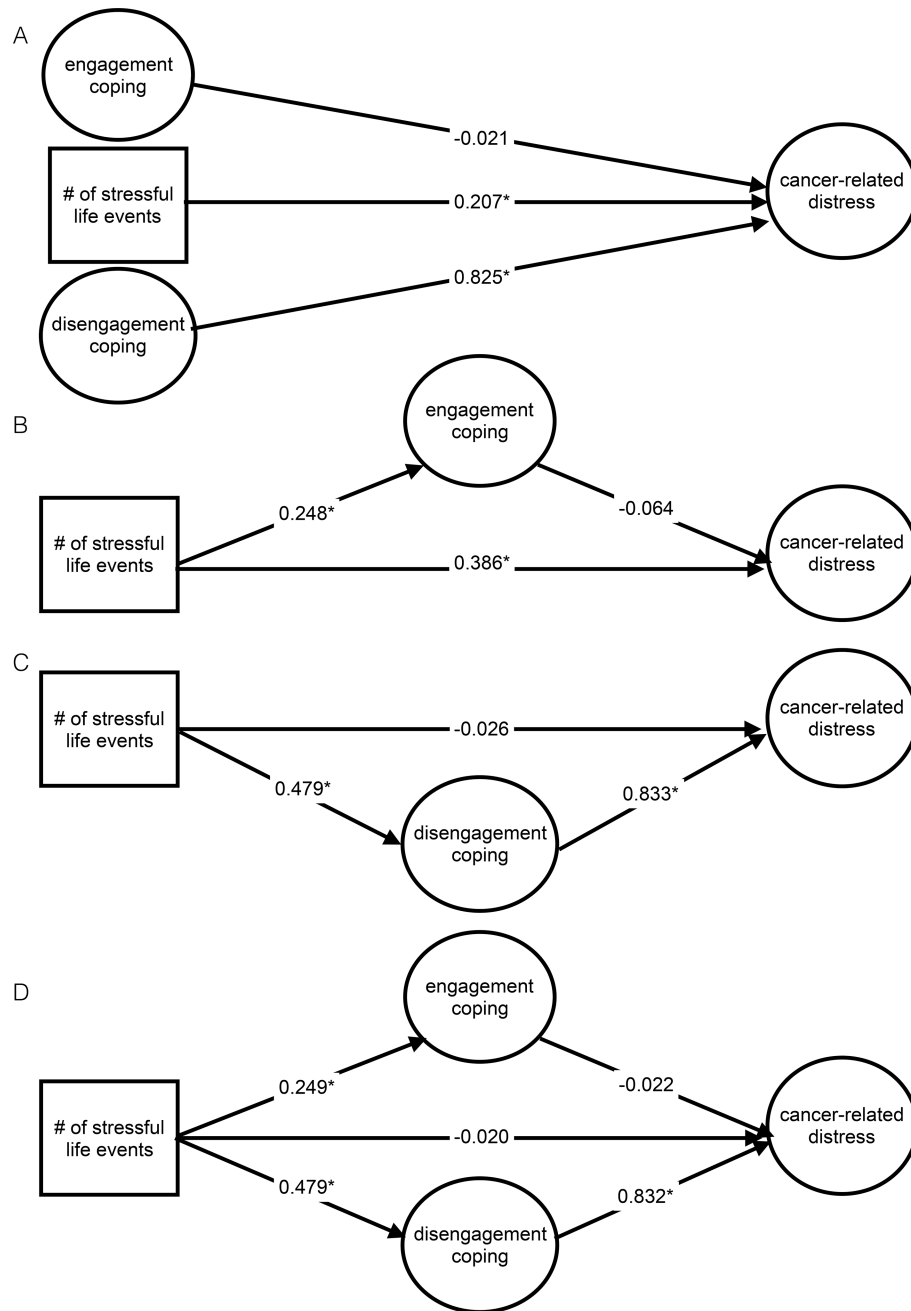


Figure 1. Structural equation models that estimated direct and indirect (mediating) effects of stressful life events (SLEs) on cancer-related distress via both engagement and disengagement coping

A: Model 1 - Direct effect of life stress (SLEs) and coping on cancer-related distress, * $p < 0.05$

B: Model 2 - Mediating effect of engagement coping on the relationship between life stress and cancer-related distress, * $p < 0.05$

C: Model 3 - Mediating effect of disengagement coping on the relationship between life stress and cancer-related distress, * $p < 0.05$

D: Model 4 - Mediating effect of both engagement and disengagement coping on the relationship between life stress and cancer-related distress, * $p < 0.05$

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Table 1

Demographic and Clinical Characteristics of the Total Sample (N= 893)

Characteristic	Mean (SD)
Age (years)	57.40 (11.97); range 19 – 90
Years of education	16.25 (2.98); range 4–23
Karnofsky Performance Status score	80.50 (12.25)
Self-administered Comorbidity Questionnaire score	6.33 (3.84)
	<u>% (N)</u>
Gender	
Female	78.5 (701)
Male	21.5 (192)
Working for pay	
Yes	34.8 (308)
No	65.2 (578)
Race/Ethnicity	
White	72.1 (628)
Asian	12.1 (105)
Black/African American	7.2 (63)
Other	8.6 (75)
Income	
<\$30,000	17.3 (138)
\$30,000–69,999	21.7 (173)
\$70,000–99,999	17.6 (140)
\$100,000	43.4 (346)
Partnered (married or living together)	
Yes	65.8 (580)
No	34.2 (302)
Type of cancer	
Breast	39.3 (351)
Gastrointestinal	29.6 (264)
Gynecologic	18.6 (166)
Lung	12.5 (112)
Metastasis to any other sites (including lymph nodes)	
Yes	68.1 (602)
No	31.9 (282)

Abbreviations: SD = Standard Deviation

Table 2

Frequency of stressful life events (in order of occurrence) and mean effect on life during past year* (N =893), based on responses to Life Stressor Checklist-Revised

Stressor	% (N)	Affected Life in Past Year** Mean (SD)	Affected Ranking
Someone close died (not suddenly)	78.2 (676)	2.19 (1.32)	11
Someone close died suddenly	50.0 (435)	2.14 (1.34)	12
Abortion/miscarriage	44.5 (309)	1.54 (1.02)	26
Been in serious disaster	41.0 (360)	1.33 (0.74)	30
Been separated/divorced	35.4 (312)	2.06 (1.35)	15
Seen serious accident	33.2 (292)	1.45 (0.82)	29
Been robbed/mugged/attacked	27.0 (236)	1.67 (1.13)	24
Seen violence in family (<16 yrs)	24.3 (212)	1.90 (1.17)	18
Cared for someone with physical/mental handicap (not child)	24.0 (208)	2.56 (1.48)	7
Had serious accident	23.8 (208)	1.57 (0.98)	25
Emotional abuse/neglect	21.8 (192)	2.59 (1.35)	6
Seen robbery/mugging/attack	21.6 (190)	1.53 (1.01)	27
Parents separate/divorce	21.3 (188)	1.79 (1.14)	21
Family member jailed	20.6 (181)	1.89 (1.36)	19
Had serious money problems	19.6 (173)	2.68 (1.66)	5
Physical (other than cancer)/mental illness	19.4 (172)	2.46 (1.36)	8
Bothered/harassed sexually	17.3 (151)	1.53 (1.00)	28
Stressful event happened to someone close	15.7 (131)	2.43 (1.40)	9
Abused/physically attacked, not sexually (<16 yrs)	15.0 (131)	1.97 (1.28)	16
Other stressful event (e.g., ill family member, combat)	12.9 (108)	3.15 (1.54)	2
Abused/physically attacked, not sexually (>16 yrs)	12.6 (110)	1.85 (1.22)	20
Touched or forced to touch sexually (<16 yrs)	12.0 (105)	2.08 (1.40)	14
Been sent to jail	6.7 (59)	1.77 (1.21)	22
Forced to have sex (>16 yrs)	6.5 (57)	1.77 (1.18)	23
Touched or forced to touch sexually (>16 yrs)	6.5 (57)	1.91 (1.18)	17
Physical neglect	4.9 (43)	2.76 (1.34)	3
Forced to have sex (<16 yrs)	4.7 (41)	2.10 (1.34)	13
Child had physical/mental handicap	3.6 (31)	3.16 (1.42)	1
Foster care/adoption	2.4 (21)	2.32 (1.49)	10
Separated from child	2.0 (17)	2.71 (1.65)	4

* Affected life: 1: "Not at all"; 3: "Some"; 5: "Extremely"

Abbreviations: SD = Standard Deviation

Table 3

LSC-R Total Endorsed Number of Stressors and Mean Effect on Past Year of Life by Demographic and Clinical Characteristics.

	LSC-R: Total Endorsed Number of Stressors Mean (SD)	p-value	LSC-R: Mean Effect on Past Year of Life Mean (SD)	p-value
Gender				
Female	6.17 (4.02)	p=0.093	1.87 (0.94)	p=0.069
Male	5.63 (3.86)		1.73 (0.90)	
Race/Ethnicity				
White (1)	6.11 (3.80)	p<0.001 1,3,4>2 4>1	1.79 (0.85)	p=0.054
Asian (2)	4.14 (3.14)		1.81 (1.14)	
Black/African American (3)	7.06 (4.31)		1.97 (1.04)	
Other (4)	7.75 (5.21)		2.07 (0.95)	
Income				
<\$30,000 (1)	7.77 (4.94)	p<0.001 1>2,3,4	2.13 (1.05)	p<0.001 1>3,4 2>4
\$30,000–69,999 (2)	6.25 (4.44)		1.94 (1.04)	
\$70,000–99,999 (3)	6.39 (3.82)		1.83 (0.87)	
\$100,000 (4)	5.40 (3.43)		1.69 (0.94)	
Married/Partnered				
Yes	5.48 (3.67)	p<0.001	1.71 (0.88)	p<0.001
No	7.16 (4.35)		2.08 (0.98)	
Metastasis to any other sites				
Yes	5.97 (3.99)	p=0.322	1.82 (0.94)	p=0.323
No	6.25 (3.96)		1.89 (0.91)	
Pearson's r			Pearson's r	
Age	0.02	p=0.495	-0.08	p=0.023
Functional status (KPS) score	-0.14	p<0.001	-0.13	p<0.001
Comorbidity score	0.24	p<0.001	0.12	p<0.001

Abbreviations: SD = Standard Deviation

Table 4

Descriptive Statistics and Correlations for Variables for Variables* in the Joint Mediation Model

	Variables							
	IES-R Total	LSC-R Total	Self-blame	Denial	Behavioral disengagement	Active coping	Positive reframing	Emotional support
N	932	904	936	930	933	930	933	934
Mean	18.5	6.05	0.853	0.502	0.243	3.95	3.4	4.28
Median	16.6	5	0	0	0	4	4	5
SD	13	3.98	1.29	1.11	0.74	1.63	1.95	1.68

Correlations with Cancer-Related Distress (IES-R Total)						
IES-R Total	Self-blame	Denial	Behavioral disengagement	Active Coping	Positive Reframing	Emotional Support
R	0.141	0.44	0.401	0.291	-0.04	-0.041
p-value	<.00005	<.00005	<.00005	<.00005	0.222	0.216
N	881	923	918	922	918	921

Correlations within coping variable sets (r/p-value/N)						
	Disengagement coping			Engagement coping		
	Self-blame	Denial	Behavioral disengagement	Active coping	Positive reframing	Emotional support
Denial	0.226		Positive reframing	0.445		
	<.00005			<.00005		
		929			927	
Behavioral disengagement	0.28	0.293	Emotional support	0.388	0.307	
	<.00005	<.00005		<.00005	<.00005	
		933	927		927	930

* Variables in the joint mediation model:

IES-R Total: Impact of Events Scale-Revised total score (Cancer-related distress)

LSC-R Total: Life Stressor Checklist-Revised total number of stressors endorsed Brief COPE Subscales:

Engagement Coping: Active Coping, Positive Reframing, Using Emotional Support
 Disengagement Coping: Self-blame, Denial, Behavioral Disengagement

Abbreviations: SD = Standard Deviation

Table 5
 Measurement Model for Cancer-Related Distress (IES-R Total) on Life Stress (LSC-R Total), Engagement Coping, and Disengagement Coping, with Life Stress Mediated by Engagement and Disengagement Coping

Outcome	IES-R Total	Raw Coefficient	SE	z	p	LL 95% CI	UL 95% CI	Standardized Coefficient
<i>Engagement Coping</i>								
Active coping	1.0	1.0						.744
Positive reframing	.965	.965	.093	10.422	<.001	.784	1.147	.600
Emotional support	.736	.736	.078	9.403	<.001	.582	.889	.532
<i>Disengagement Coping</i>								
Self-blame	1.0	1.0						.561
Denial	.747	.747	.133	5.606	<.001	.486	1.009	.487
Behavioral disengagement	.411	.411	.073	5.621	<.001	.268	.554	.401
<i>IES-R Total</i>								
IES-R Total	.694	.694	.123	5.654	<.001	.454	.935	.954
Corrected Residual								
Denial with Behavioral disengagement	.085	.085	.038	2.216	.027	.010	.160	.129

Abbreviations: SE = Standard Error; LL = Lower Limit; UL = Upper Limit; CI = Confidence Interval; IES-R = Impact of Events Scale – Revised; LSC-R = Life Stressor Checklist – Revised

Table 6

Structural Model for Cancer-Related Distress (IES-R Total) on Life Stress (LSC-R Total), Engagement Coping, and Disengagement Coping, with the Effect of Life Stress Mediated by Engagement and Disengagement Coping

Outcome	IES-R Total	Raw Coeff.	SE	z	p	LL 95% CI	UL 95% CI	Std. Coeff.
Structural Models								
LSC-R Total	IES-R Total	-.036	.229	-1.57	.875	-.485	.413	-.020
Engagement coping		-.032	.055	-.581	.561	-.141	.076	-.022
Disengagement coping		2.068	.727	2.846	.004	.644	3.493	.832
Engagement coping on:								
LSC-R Total		.302	.118	2.565	.010	.071	.533	.249
Disengagement coping on:								
LSC-R Total		.346	.127	2.721	.007	.097	.596	.479
Mediation Model								
Total Effect		Raw Coeff.[‡]				LL 95% BC* CI	UL 95% BC* CI	
LSC-R Total		0.671				.304	1.432	n/a
Indirect (Mediating) Effects		Raw Coeff.[‡]				LL 95% BC* CI	UL 95% BC* CI	
Total Indirect		.707				.230	2.206	n/a
LSC-R Total via Engagement coping		-.010				-.066	.022	n/a
LSC-R Total via Disengagement coping		.716				.238	2.244	n/a
Model Fit Indices^{**}								
Chi-Square Test of Model Fit		62.084, 16df						
		P<.00005						
RMSEA		.057						
CFI		.934						
SRMR		.042						

[‡]Nonparametric bootstrapped estimate, with 5,000 repetitions

* Nonparametric bootstrapped 95% bias-corrected confidence interval, with 5,000 repetitions. If zero is not in the interval, the coefficient is significant.

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Significant Chi-squared expected due to large sample size; RMSEA < .06 preferred; CFI > .90 acceptable; SRMR < .08 preferred. The model meets the three primary criteria for good fit.

Abbreviations: SE = Standard Error; LL = Lower Limit; UL = Upper Limit; CI = Confidence Interval; IES-R = Impact of Events Scale – Revised; LSC-R = Life Stressor Checklist – Revised; Std = Standardized; Coeff = Coefficient; BC = Bias-Corrected; RMSEA = Root Mean Squared Error of Approximation, CFI = Comparative Fit Index; SRMR = Standardized Root Mean Squared Residual; df = Degrees of Freedom